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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| 08/980,395 | 11/28/97 | SONTHEIMER H | D5858D1 |

| EXAMINER | |
|---|---|
| HUFF S | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | 29 |

HM12/0924
MORGAN, LEWIS, AND BOCKIUS,LLP
1800 M STREET, N.W.
WASHINGTON DC 20036

**DATE MAILED:** 09/24/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. 08/980,395 | Applicant(s) SONTHEIMER ET AL. | |
|---|---|---|---|
| | Examiner Sheela J Huff | Art Unit 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 21-39 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 21-39 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Response to Amendment*

The amendment filed on 7/30/01 has been considered. Applicant's arguments are deemed to be persuasive-in-part.

Claims 21-39 are pending.

The rejection under 35 U.S.C. 112, first paragraph, is withdrawn in view of applicant's amendment.

The rejection of claims 30-31 under 35 USC 101 should have been and obviousness-type double patenting rejection and this Office Action reflects this.

All of the art rejections have been withdrawn in view of applicant's amendment.

### *Response to Arguments*
### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 28 and 30-31 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 6028174. The reasons for this rejection are of record in paper no. 26, mailed 3/29/01.

Applicant indicates that a terminal disclaimer will be filed when allowable subject matter is indicated.

***New Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

Claims 38 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 38, the terminology "glial-derived" is vague and indefinite. What does applicant mean by "derived"?

Claims 21-39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in In Re Colianni, 195 USPQ 150 (CCPA 1977) and have been adopted by the Board of Patent Appeals and Interferences in Ex Parte Forman, 230 USPQ 546 (BPAI 1986). Among these factors are:

1. the nature of the invention,
2. the state of the prior art,

3. the predictability or lack thereof in the art,
4. the breath of the claims,
5. the amount of direction or guidance present, and
6. the presence or absence of working examples.

The following is an analysis of these factors in relationship to this application.

Nature of the invention

Applicant claims a pharmaceutical composition comprising chlorotoxin and wherein the use of the of the composition is in humans.

State of the Art

While the state of the art does show that compositions comprising chlorotoxin can be used in arthropods (see DeBin et al Am. J. Physiol. Vol. 264/2 p. C361 (1993), there is no objective evidence of record that the composition can be used in vivo in humans (a showing of use in humans would be a correlation of the data provided in the specification to human use). However, the state of the art does not recognize that the claimed compounds or even analogous compounds can readily be used in vivo in humans.

Predictability

Again the claims are directed to in vivo treatments and such treatments, in and of themselves, are unpredictable because pharmacokinetic factors such as the stability of the peptides in the body, half-life, absorption efficiency, binding affinity for target cells, biotransformation, and the rate of clearance from the body are important consideration for the efficacy of the claimed subject matter and yet have not been considered. In the absence of these considerations, there is no assurance (ie. it is unpredictable) that the active peptide would be available in effective doses at the target sites and for periods of time sufficient to effect the required cellular or biological responses.

Furthermore, the data provided in the specification and the intended use of the composition is in the treatment of tumors in the brain. It is well known that blood brain barrier is a "stringent gatekeeper" between the blood and the brain ( Goldstein et al Scientific American vol. 255 p. 74 (1986)) and there is no objective evidence of record to show that the peptide in the claimed pharmaceutical composition can actually cross the blood brain barrier.

Thus, for these reasons and because there is no evidence of record to demonstrate that analogous compounds can readily be used in humans, the art is relatively unpredictable.

Guidance/Working Examples

In the case before us the bulk of the specification, though highly detailed, is devoted mainly to the description of how to make the claimed compounds. Applicant also provides several in vitro assays and an in vivo assay in mice. For the reasons discussed above, the in vitro assays are not correlatable to in vivo use. The in vivo assay requires the intracranial injection of the composition and the use of such a drastic measure for injecting the composition into a human is not favorable. Thus, the only other route of administration of the composition would be through the blood brain barrier and for the reasons discussed above, this is very difficult.

In view of the above, it is the Examiner's position that one skilled in the art could not use the invention without undue experimentation.

***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 703-305-7866. The examiner can normally be reached on M,Th 5:30 am-2:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Sheela J Huff
Primary Examiner
Art Unit 1642

sjh
September 20, 2001